

**Amendments to the Specification:**

Please add the following paragraph at page 8, after the paragraph stating "Figure 2. PEO monomer detection efficiency as a function of weight fraction":

--Figure 3. Illustration of an embodiment of a mass spectrometry ionization method.--

Please replace the paragraph beginning at page 7, line 21, with the following paragraph:

-- In another aspect, the invention further provides for directing the charged analyte through the interface of the mass spectrometer in synchrony with the duty cycle of the ion detector. The analyte may be deposited upon discrete apices of the sample surface. The sample may be bacteria, viruses or cells. The ion beam may be protons, lithium ions, cesium ions, anions, such as NH<sub>2</sub><sup>-</sup> or H<sub>3</sub>Si<sup>-</sup>, or electrons. The sample may be injected directly into the focusing ~~quadrupoles~~ quadrupoles. In a preferred embodiment, the ion beam flux may be from about 1 mA/cm<sup>2</sup> to about 17 mA/cm<sup>2</sup> and the ion beam energy may be from about 5 to about 50 electron volts, preferably from about 5 to about 10 electron volts. However, a higher ion flux may be used provided the ion detector does not become saturated.--

Please replace the paragraph beginning at page 13, line 22, with the following paragraph:

-- By moving the spray tip past the nozzle and skimmer, so that the sample is injected directly into the focusing ~~quadrupoles~~ quadrupoles, we further demonstrated negligible losses to the vacuum pump or inner surfaces of the detector. It is in the nozzle and interface region where the mean free ion path is the shortest and the potential for ion entrainment in the neutral gas stream is the greatest. In these experiments, conducted with the same peptide mix described above, we obtained detection efficiencies in the 0.01 to 1 ppb range. While this is lower than previous results, further testing revealed that this difference was entirely attributable to analyte adsorption to the inner walls of the long (up to 250 cm) uncoated capillaries used for sample introduction. --

Please replace the paragraph beginning at page 13, line 31, with the following paragraph:

-- Detector duty cycle in orthogonal TOF detectors is fundamentally limited by flight time of the ions and is about 20%, according to Applied Biosystems (ABI), the manufacturer of our current Mariner™ (ESI-TOF) system. Axial TOF and FT-ICR systems may be used to increase the detection efficiency since all the ions are collected and released at once to the sensor element. However, ICR duty cycles are limited by the mass accuracy desired, with increased time in the ICR higher mass resolution is obtained but at the expense of the overall duty cycle of the analyzer. Similarly, tandem or triple ~~quadrupole~~ quadrupole analyzers may also appear to improve detection sensitivity, because ions may be accumulated for a long time from the source before being released to the ion detector. In applications where mass accuracy is not critical, axial TOF detectors may be used, which intrinsically count all the ions reaching the sensor element. ABI independently estimates the overall transmission efficiency of their Mariner

platform at  $\geq 0.1\%$ . This is consistent with transmission efficiencies cited by others. (Belov, M.E. et al., J Am Soc Mass Spectrom, 11:19-23 (2000); Martin S.E., J. Shabanowitz, D.F. Hunt, and J.A. Marto., Anal Chem, 72:4266-4274 (2000)). Aside from the duty cycle of the detector element, our experiments suggest that ionization efficiency is the major source of ion loss through the MS process.--